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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/788,552	02/21/2001	Serge Braun	032751-053	5627

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EXAMINER

SHUKLA, RAM R

ART UNIT PAPER NUMBER

1632

DATE MAILED: 01/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/788,552

Applicant(s)

BRAUN, SERGE

Examiner

Ram R. Shukla

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 20 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24, 43 and 46-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24, 43 and 46-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 February 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

1. Amendments and response filed 11-202003 have been received and entered.
2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on **11-20-2003** has been entered.
3. Claims 24, 43 and 46-51 are pending and under consideration.
4. The enablement rejection of claim 24 has been withdrawn in view of amendments to the claim wherein the naked DNA is directly administered to the muscle cells.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 24 and 46-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Triantaphyllopous et al (Gene Therapy 5:253-263, 1998) in view of Youssef et al (The Journal of Immunology 161:3870-3879, 1998), Felgner et al (US Patent 5,580,859, 12-3-1996), Lemieux et al (US 6,359,054 B1, 3-19-2002, effective filing date 11-18-1994).

At the time of the invention, Triantaphyllopous et al taught a vector for expression of interferon beta and a method for introducing the vector in mice model of EAE (see the methods section on page 259, left and right columns, results section on page 257, left column and discussion). The art also taught that IFN-beta had a beneficial effect on the disease course in relapsing-remitting multiple-sclerosis (MS) patients, shown by reductions in both the magnetic resonance imaging lesions and the severity and frequency of relapse (see the second paragraph of introduction in column 1 continued in column 2). The art also taught intracranial injection of IFN beta vector to mice before the onset of EAE and that the LTR driven IFN beta was more efficient in blocking disease severity compared to NSE promoter driven INFN beta. The art also teaches that feasibility of expressing IFN-beta by gene therapy in animal models of human disease will help to clarify its role in pathogenesis and its mechanism of action in therapeutic interventions of autoimmune diseases, cancer etc (see the discussion on page 257, right column). This art does not teach treatment of MS by administering a naked DNA expressing beta-interferon in a patient.

Youssef et al teaches a DNA vaccination with chemokines for treating EAE (see the abstract and the methods section). They further teach the novelty of DNA vaccination in expressing foreign antigens as well as for expressing cytokines (see the discussion in the second column on page 3877).

At the time of the invention, it was routine in the art to directly administer naked DNA molecules to tissues for providing a therapeutic protein for treating diseases and for vaccination (see Felgner et al). Lemieux et al taught DNA compositions for intramuscular injections. The art also teaches expression of

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interferons by direct injection in the muscles (see column 22, lines 29-67 continued in column 23 and examples 41-48).

At the time of the invention, it would have been obvious to an artisan of ordinary skill in the art to directly inject a naked DNA vector expressing IFN-beta to the muscles of a MS patient with a reasonable expectation of success. An artisan would have been motivated to treat MS by directly injecting naked DNA encoding IFN-beta into muscle because direct DNA injection is simple and naked DNA was known to work for expressing other proteins related to MS development, direct injection produces both humoral and cellular responses (see abstract and the rest of the article of Youssef et al) and because the unique cytoarchitectural features of muscle tissue help in better uptake of polynucleotides and express injected DNA vector relative to other tissues (see Lemieux et al, column 1, lines 20-32) .

Regarding claims 46-51, it is noted that use of promoters, polyA site and enhancer elements in vectors was routine in the art at the time of the art. Similarly, effective amount of 1 ug to 1 g is a broad range and it was routine in the art to standardize the amount of any pharmaceutical composition for optimal therapeutic benefits.

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for TC 1600 is (703) 703-872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

Please note that effective January 13, the offices for Examiner Shukla, SPE Reynolds and LIE William Phillips will move to the new USPTO location in

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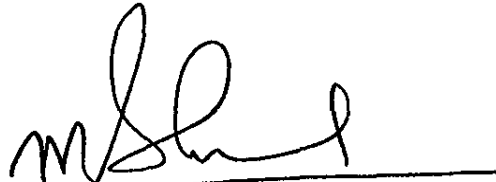
Alexandria, VA and their phone numbers will change. The new phone numbers will be as follows:

Ram Shukla: **(571) 272-0735**

Deborah Reynolds: **(571) 272-0734**

William Phillips: **(571) 272-0548**

Ram R. Shukla, Ph.D.
Primary Examiner
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A handwritten signature in black ink, appearing to read 'R. Shukla', written over a horizontal line.

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER